

REMARKS

This amendment supplements the amendment filed October 3, 2001, on which applicants continue to primarily rely.

The confusion regarding claim 19 is sincerely regretted. Claim 19 was both indicated as being canceled and amended in the amendment filed October 3, 2001. As applicants had intended to amend claim 19, the indication that claim be canceled is in error.

With regard to amending claims 27-29, 31, and 33 to define an acceptable carrier as being "pharmaceutically" acceptable, it is submitted that this in no way is intended to direct the composition to be limited to pharmaceutical compositions, rather, it merely sets forth clearly that the carrier be a pharmaceutically acceptable carrier.

Favorable consideration and allowance are respectfully solicited.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 1, 8, 16, 17, 20, 27-29, 31-33, and 34 have been amended as follows:

1 (Twice-Amended). A non-hemolytic cytolytic peptide having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity, said non-hemolytic cytolytic peptide being selected from the group consisting of:

- (A) a cyclic derivative of a peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising one or both of L-amino acid residues and D-amino acid residues, and comprising an α -helix breaker moiety;
- (B) a peptide comprising both L-amino acid residues and D-amino acid residues, having a net positive charge which is greater than +1, and having a sequence of amino acids such that a corresponding amino acid sequence comprising only L-amino acid residues is not found in nature, and cyclic derivatives thereof;
- (C) a complex consisting of a plurality of 2 or more non-hemolytic cytolytic peptides, each peptide having a net positive charge

which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising one or both of L-amino acid residues and D-amino acid residues and comprising an α -helix breaker moiety, or cyclic derivatives of the foregoing, said peptides being linked together by the use of a linker molecule covalently bound to each of the peptides; and

- (D) a random copolymer consisting of ~~a ratio of~~ a hydrophobic, a positively charged and a D-amino acid.

8(Twice-Amended). The peptide according to claim 7, having the following characteristics:

- (a) it is a non-natural synthetic peptide composed of ~~a ratio of~~ at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid;
- (b) the peptide has a net positive charge which is greater than +1; and
- (c) ~~the ratio of hydrophobic to positively charged amino acids is such that~~ the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells.

16(Twice-Amended). The complex according to claim 15, which is composed of 2 or more, molecules of the same peptide or of different peptides, and the linker is:

- (a) a cyclic derivative of a peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising one or both of L-amino acid residues and D-amino acid residues, and comprising an α -helix breaker moiety;
- (b) a peptide comprising both L-amino acid residues and D-amino acid residues, having a net positive charge which is greater than +1, and having a sequence of amino acids such that a corresponding amino acid sequence comprising only L-amino acid residues is not found in nature, and cyclic derivatives thereof; or
- (c) a commonly used linker.

17(Thrice-Amended). The complex according to claim ~~13~~36, wherein the linked Lys/Leu diastereomers are herein designated 96 and 97 ~~are covalently linked together through a linker molecule:~~

96. ($[D]-L^{3,4,8,10}-K_4L_8C$)₅ $[D]-L^{3,4,8,10}-K_4L_8$ of the sequence:

(Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-Cys-NH₂)₅
Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂ (SEQ ID NOS: 96 and 23)

97. ($[D]-L^{3,4,8,10}-K_5L_7C$)₅ $[D]-L^{3,4,8,10}-K_4L_9$ of the sequence:

(Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-Cys-NH₂)₅ Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH₂ (SEQ ID NOS: 97 and 24).

20 (Twice-Amended). The non-hemolytic cytolytic random copolymer according to claim 1(D), consisting of ~~different ratios of~~ a hydrophobic, a positively charged and a D-amino acid.

27 (Once-Amended). A composition comprising ~~an~~ a pharmaceutically acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit bacterial growth.

28 (Once-Amended). A composition comprising ~~an~~ a pharmaceutically acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit growth of fungi.

29 (Once-Amended). A composition comprising ~~an~~ a pharmaceutically acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit proliferation of cancer cells.

31 (Once-Amended). A composition comprising ~~an~~ a pharmaceutically acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit a viral activity.

33 (Once-Amended). A composition comprising ~~an~~ a pharmaceutically acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit growth of a protozoan.

34(Once-Amended). A mixture consisting of two or more non-hemolytic cytolytic peptides or cyclic derivatives thereof, each peptide having a net positive charge which is greater than +1 and comprising both L-amino acid residues and D-amino acid residues, or each ~~selected from the group consisting of a peptide according to claim 1, a peptide comprising one or both of L-amino acid residues and D-amino acid residues and comprising an α -helix breaker moiety,~~ and a cyclic derivatives thereof.